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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/035,091	12/21/2001	Holly Hogrefe	25436/2152	1719
27495 7590 05/01/2007 PALMER & DODGE, LLP KATHLEEN M. WILLIAMS / STR 111 HUNTINGTON AVENUE BOSTON, MA 02199			EXAMINER HUTSON, RICHARD G	
			ART UNIT 1652	PAPER NUMBER
			MAIL DATE 05/01/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/035,091

Applicant(s)

HOGREFE ET AL.

Examiner

Richard G. Hutson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 February 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 10-14, 20, 22-26 and 30-51 is/are pending in the application.
- 4a) Of the above claim(s) 23-26 and 30-35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 10-14, 20, 22 and 36-51 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/15/2007 has been entered.

Applicant's amendment of claims 1, 3, 10, 12, 14, 22 and 36-50, in the paper of 2/15/2007, is acknowledged and has been entered. Applicants' arguments filed on 2/15/2007, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Claims 1-3, 10-14, 20, 22-26, and 30-51 are still at issue and are present for examination

Claims 23-26 and 30-35 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Objections

Claims 1 is objected to because of the following informalities:

Claims 1 recites "...G387, and G388, and...". It is suggested that each of the commas preceding "and" be deleted.

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Claim 37 does not read properly. It appears that the "consisting of" should be "consists", however this would not correct 112 second paragraph issues raised below.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 10-14, 20, 22 and 36-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (2, 3, 10-14, 20 and 22 dependent on), 36 (37-39 dependent on), 40 (41-43 dependent on), 44 (45-47 dependent on), 48, 49, 50 (51 dependent on) are each indefinite in that it is confusing and unclear in the recitation "said second enzyme is Pfu DNA polymerase consisting of an amino acid substitution at an amino acid position selected from the group consisting of: Y410, T542, D543, K593, Y595, G387, and G388". This recitation is unclear in that Pfu DNA polymerase does not "consist of an amino acid substitution", but rather Pfu DNA polymerase is an approximate 700 amino acid protein isolated from *Pyrococcus furiosus*. It is believed that use of the word "consisting" in this context is incorrect and thus unclear. It is suggested that an amendment such as "said second enzyme is Pfu DNA polymerase, except that it is mutated at an amino acid position selected from the group consisting of: Y410, T542, D543, K593, Y595, G387, and G388" would be clearer and helpful in claiming the

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subject invention. This is further illustrated in claims 41-43 which each recite "Pfu DNA polymerase comprises..." yet also depend from claim 40 which recites "Pfu DNA polymerase consisting of".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 10, 11, 12, 20 and 22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection was stated in the previous office action as it applied to previous claims 1, 10-12, 20, 22, 36-39, 40-43, 44-47 and 48-51. In response to the rejection, applicants have amended claims 1, 3, 10, 12, 14, 22 and 36-50 and traverse the rejection as it applies to the newly amended claims.

Applicants traverse this rejection on the basis that applicants have amended the claims to recite a first enzyme comprising "5'-3' polymerization activity of a DNA polymerase or reverse transcriptase" thus clarifying that the activity possessed by the claimed enzyme is the DNA polymerization activity itself. Applicants submit that the specification teaches over 30 examples of enzymes that possess the 5'-3' DNA polymerization activity of a DNA polymerase or reverse transcriptase and that based

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upon the disclosure and the state of the art at the time the instant application was filed, applicants have demonstrated that they were in possession of the invention recited in the amended claims and accordingly request that the rejection be reconsidered and withdrawn

Applicant's complete argument is acknowledged and has been carefully considered, however, continues to be found non-persuasive on the following basis. It is noted that applicants claims as amended recite "said first enzyme comprises 5'-3' polymerization activity of a DNA polymerase or reverse transcriptase". It is further noted that applicants argue that applicant's specification teaches that all DNA polymerases possess 5'-3' DNA polymerization activity. It remains that applicants have not adequately described those enzymes of the claim comprising any enzyme which comprises a 5'-3' polymerization activity of a DNA polymerase or reverse transcriptase beyond those enzymes which are a DNA polymerase or reverse transcriptase. As claim 2 is drawn to the enzyme mixture of claim 1, wherein said first enzyme is a DNA polymerase or reverse transcriptase, it would appear that claim 1 is drawn to those enzyme mixtures which in addition to DNA polymerases and reverse transcriptases, includes enzymes which possess 5'-3' polymerization activity and are not DNA polymerases or reverse transcriptases. Applicants have not described a single enzyme which possess a 5'-3' polymerization activity and are not either a DNA polymerase or a reverse transcriptase.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1, 10, 11, 12, 20 and 22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an enzyme mixture comprising a first and second enzyme, wherein said first enzyme is a DNA polymerase or reverse transcriptase and said second enzyme is a Pfu DNA polymerase which comprises the amino acid sequence of SEQ ID NO: 19 with a mutation selected from the group consisting of Y410, T542, D543, K593, Y595, Y385, G387 and G388, does not reasonably provide enablement for an enzyme mixture comprising a first and second enzyme, wherein said first enzyme comprises a 5'-3' polymerization activity of a DNA polymerase or reverse transcriptase and said second enzyme is a mutant Pfu DNA polymerase consisting of an amino acid substitution at an amino acid position selected from the group consisting of: Y410, T542, D543, K593, Y595, Y385, G387 and G388. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection was stated in the previous office action as it applied to previous claims 1, 10-12, 20, 22, 36-39, 40-43, 44-47 and 48-51. In response to the rejection, applicants have amended claims 1, 3, 10, 12, 14, 22 and 36-50 and traverse the rejection as it applies to the newly amended claims.

Applicants traverse this rejection on the basis that applicants have amended the claims to recite a "Pfu DNA polymerase consisting of an amino acid substitution at an amino acid position selected from the group consisting of" the specified sites of mutation and as amended, the claims no longer encompass amino acid substitutions in a Pfu DNA polymerase other than at the specified amino acid positions. Applicants submit that applicants should not have to include a particular sequence in the claims, as applicants submit that the sequence of Pfu DNA polymerase can be accessed in the Swissprot database at accession number P80061, as well as in four specifically referenced U.S. patents. Applicants note that the sequence of the Pfu DNA polymerases taught in each of the four patent references and P80061 is the same.

Applicant's complete argument is acknowledged and has been carefully considered, however, continues to be found non-persuasive on the following basis. It is noted that applicant's amendment as discussed above under 112 second paragraph regarding the Pfu DNA polymerase is indefinite in that it is unclear. This recitation is unclear in that Pfu DNA polymerase does not "consist of an amino acid substitution", but rather Pfu DNA polymerase is an approximate 700 amino acid protein isolated from *Pyrococcus furiosus*. It is believed that use of the word "consisting" in this context is incorrect and thus unclear. It is suggested that an amendment such as "said second enzyme is Pfu DNA polymerase, except that it is mutated at an amino acid position selected from the group consisting of: Y410, T542, D543, K593, Y595, G387, and G388" would be clearer and helpful in claiming the subject invention.

Additionally, applicants claims remain rejected for a lack of enablement because applicants have not enabled those first enzymes beyond DNA polymerases and reverse transcriptases that have a 5'-3' polymerization activity of a DNA polymerase or reverse transcriptase. As discussed above under the above description rejection, applicants have described those enzymes which have a 5'-3' polymerization activity of a DNA polymerase or reverse transcriptase, wherein said enzyme is a DNA polymerase or a reverse transcriptase, however, applicants have not given guidance as to any enzyme that has such an activity that are not a DNA polymerase or a reverse transcriptase.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any enzyme mixture comprising any Pfu DNA polymerase with the specified mutations. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of enzymes having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Double Patenting

Applicants comments in response to the previous statutory type double patenting rejection regarding the canceling of the subject matter of claims 1-3, 6, 9-11, 13-15, 19 and 21-23 of copending application 10/079,241 are acknowledged, however it is further

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acknowledged that applicants along with the cancellation of claims 1-3, 6, 9-11, 13-15, 19 and 21-23 of copending application 10/079,241, added new claims 64-87 drawn to overlapping subject matter, thus necessitating a provisional nonstatutory double patenting rejection.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3, 10-14, 20, 22 and 36-51 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 64-70, 75-87 of copending Application No. 10/079,241. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claimed enzyme mixtures of the instant application, comprising a first enzyme and a second enzyme wherein said first enzyme comprises a DNA polymerization activity and said second enzyme is a mutant Pfu DNA polymerase having a mutation at an amino acid position selected from the group consisting of D405, Y410, T542, K593, Y595, Y385, Y387, and G388 and those further limited claims dependent thereon are anticipated by and thus obvious over the corresponding claims of copending Application No.

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10/079,241, drawn to a enzyme mixture comprising a first enzyme and a second enzyme wherein said first enzyme is an Archaeal DNA polymerase and said second enzyme is a mutant Archaeal DNA polymerase having a mutation at an amino acid position selected from the group consisting of D405, Y410, T542, K593, Y595, Y385, Y387, and G388 and those further limited claims dependent thereon.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant acknowledgment of this provisional rejection is acknowledged, as well as applicant's statement of their intent of filing a terminal disclaimer as a means of overcoming the rejection at the time at which the claims are found otherwise allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read 'R. G. Hutson', with a long horizontal line extending to the right.

Richard G Hutson, Ph.D.
Primary Examiner
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rg
6/8/2006